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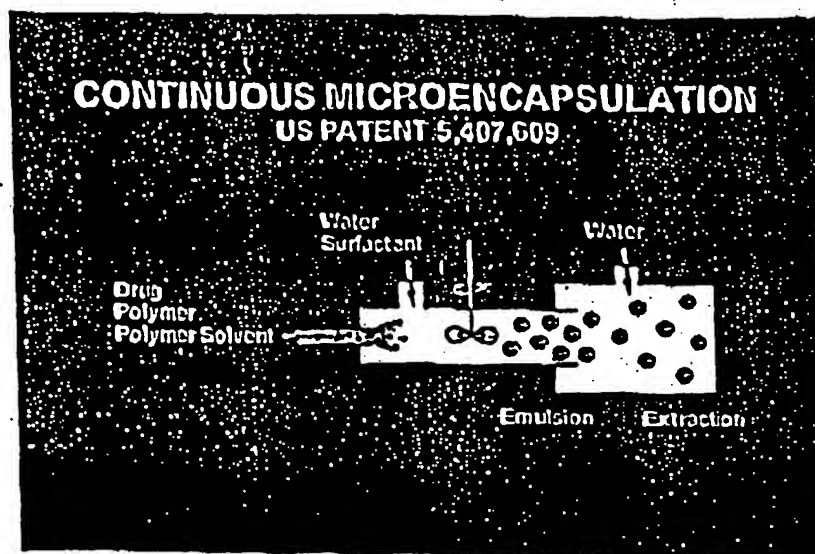
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SOUTHERN RESEARCH'S PATENTED MICROENCAPSULATION PROCESS



Advantages

- US Patent issued 1995
- Fast encapsulation time -- milliseconds
- Minimal exposure to polymer solvent
- High encapsulation efficiency
- Good Yields
- Makes small microparticles
 <100 micron <10 micron

Drugs Microencapsulated

- Proteins
- Peptides
- Small molecules
- Water-soluble drugs
- Hydrophobic drugs
- Drugs encapsulated in
 lactide/glycolide polymers

FIGURE 1

FIGURE 2.

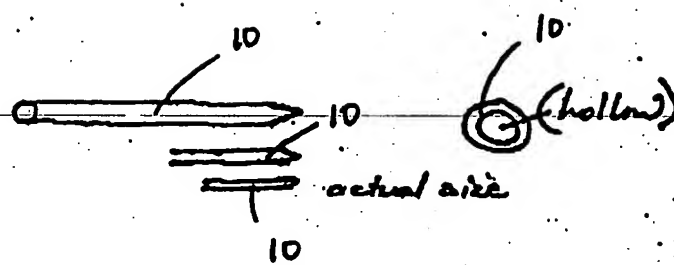
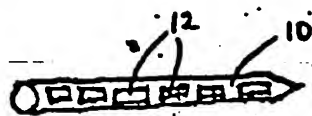


FIGURE 3



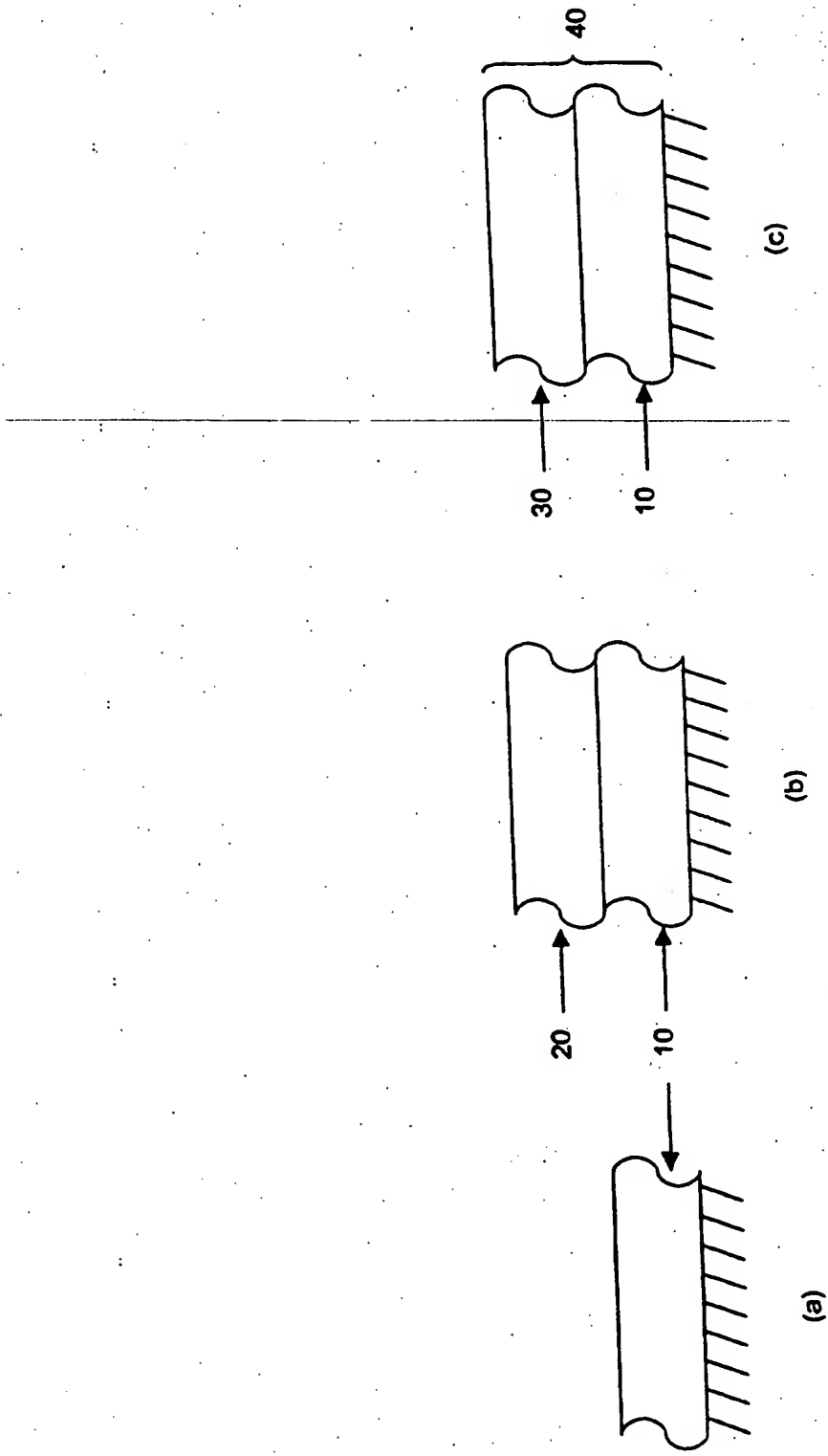


FIGURE 4

Conditions: Ambient

Material:	PX510	PX261	PX749	PX125	PX510 + 14% Paclitaxel
Hardness:	F	B	3B	4B	F

Conditions: 5 minutes in 37°C pH 7.4 Saline Buffer

Material:	PX510	PX261	PX749	PX125	PX510 + 14% Paclitaxel
Hardness:	F	B	9B	<9B	F

Hardness Rating: 2H-H-F-HB-B-2B-3B-4B-5B-6B-7B-8B-9B
 Harder ← → Softer

FIGURE 5

Conditions: Ambient

Material:	PX510	PX261	PX749	PX125	PX510 + 14% Paclitaxel
Resistance To Cracking	< 3 mm	< 3 mm	< 3mm	< 3mm	< 3mm

Conditions: 5 minutes in 37°C pH 7.4 Saline Buffer

Material:	PX510	PX261	PX749	PX125	PX510 + 14% Paclitaxel
Resistance To Cracking	< 3 mm	< 3 mm	< 3mm	< 3mm	< 3mm

FIGURE 6

Conditions: Ambient

Material:	PX510	PX261	PX749	PX125	PX510 + 14% Paclitaxel
Class:	5B	5B	5B	4B	5B

Class Rating: 5B = 0% of coating removed from substrate
4B = Less than 5% of coating removed from substrate

FIGURE 7

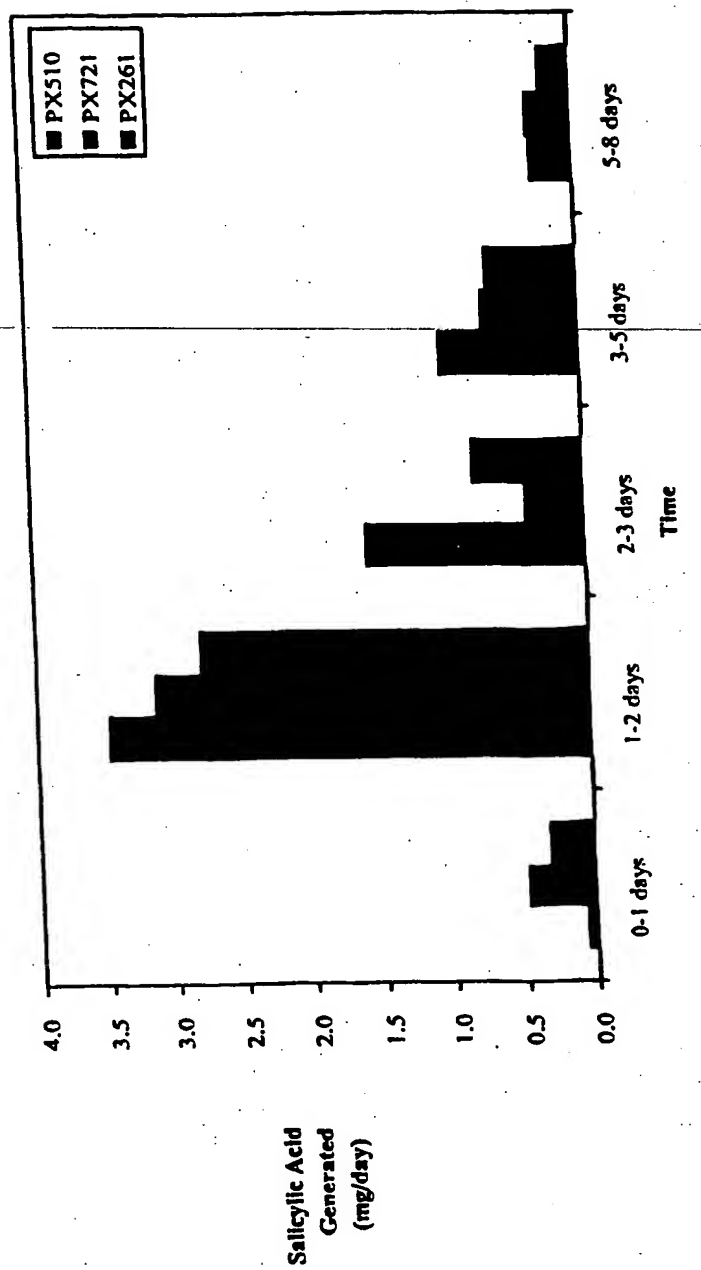


FIGURE 8A

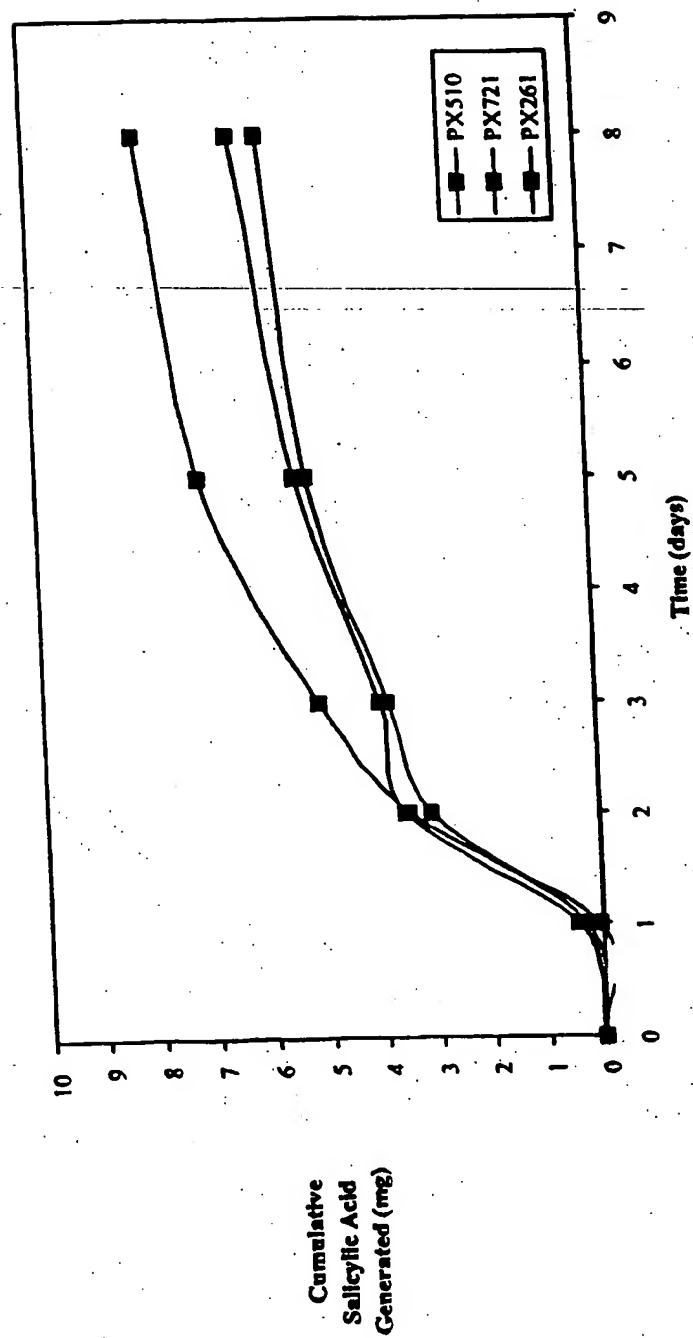


FIGURE 8B

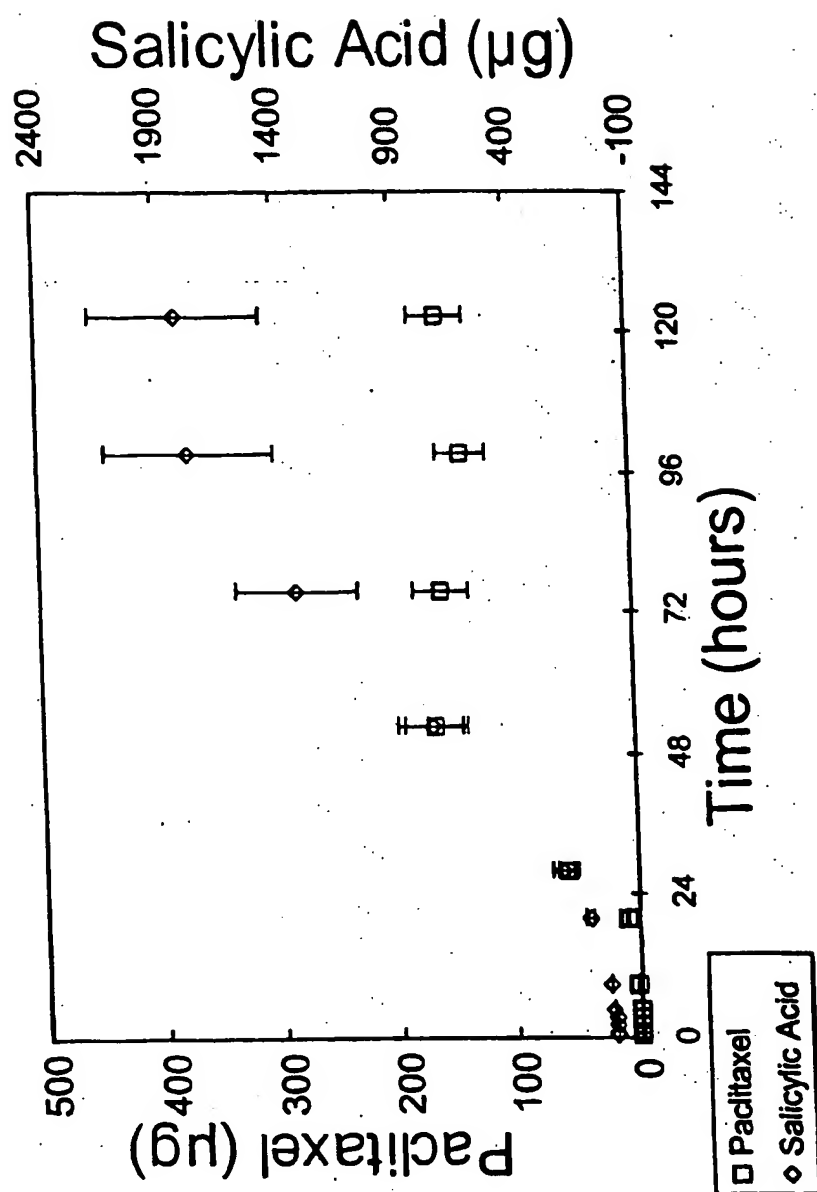


FIGURE 9A

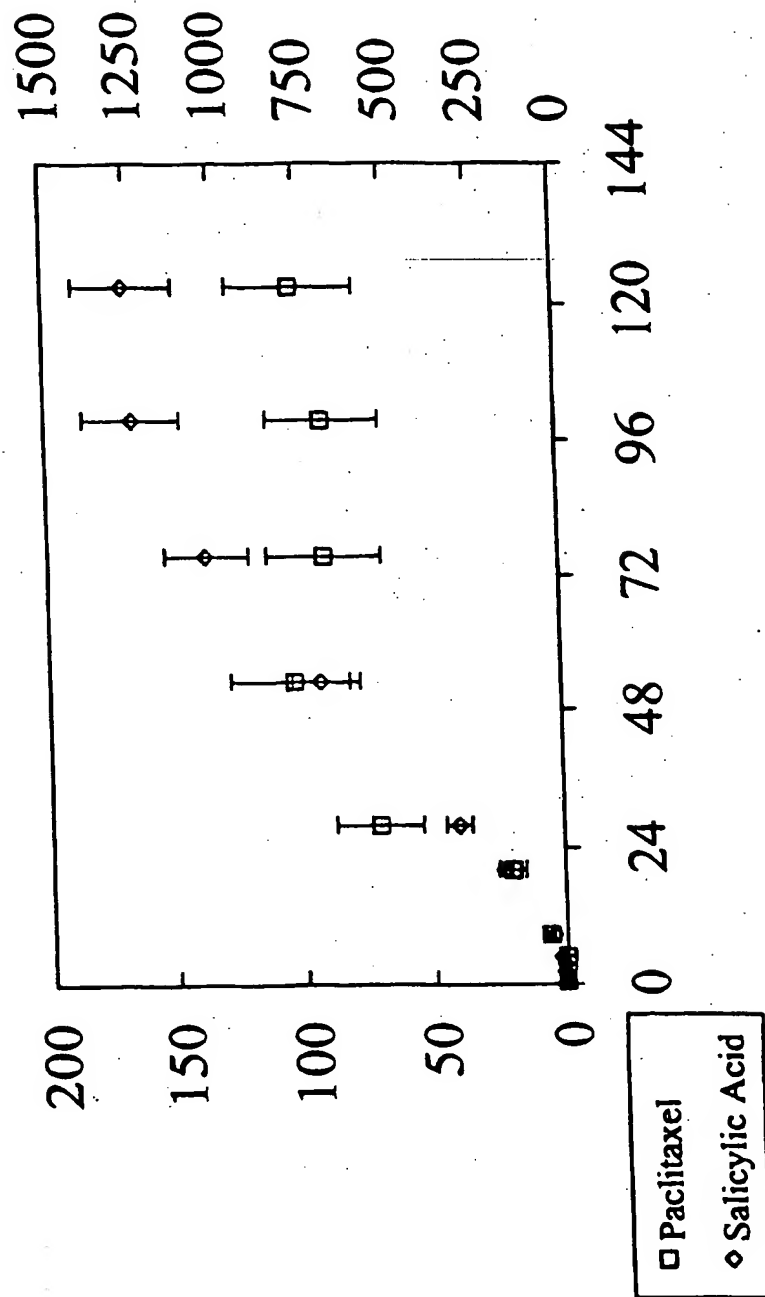


FIGURE 9B

Formulation

Property	PX510	PX721	PX261	PX749
T_g (C)	44	38	29	16
Tensile modulus (MPa)	2.0 (25 C) 5.1 (37 C)			3.0 (25 C)
Yield Strength (MPa)	Not observed			6.0 (25 C)
Ultimate Elongation (%)	1.5 (25 C) 350 (37 C)			500 (25 C)

FIGURE 10

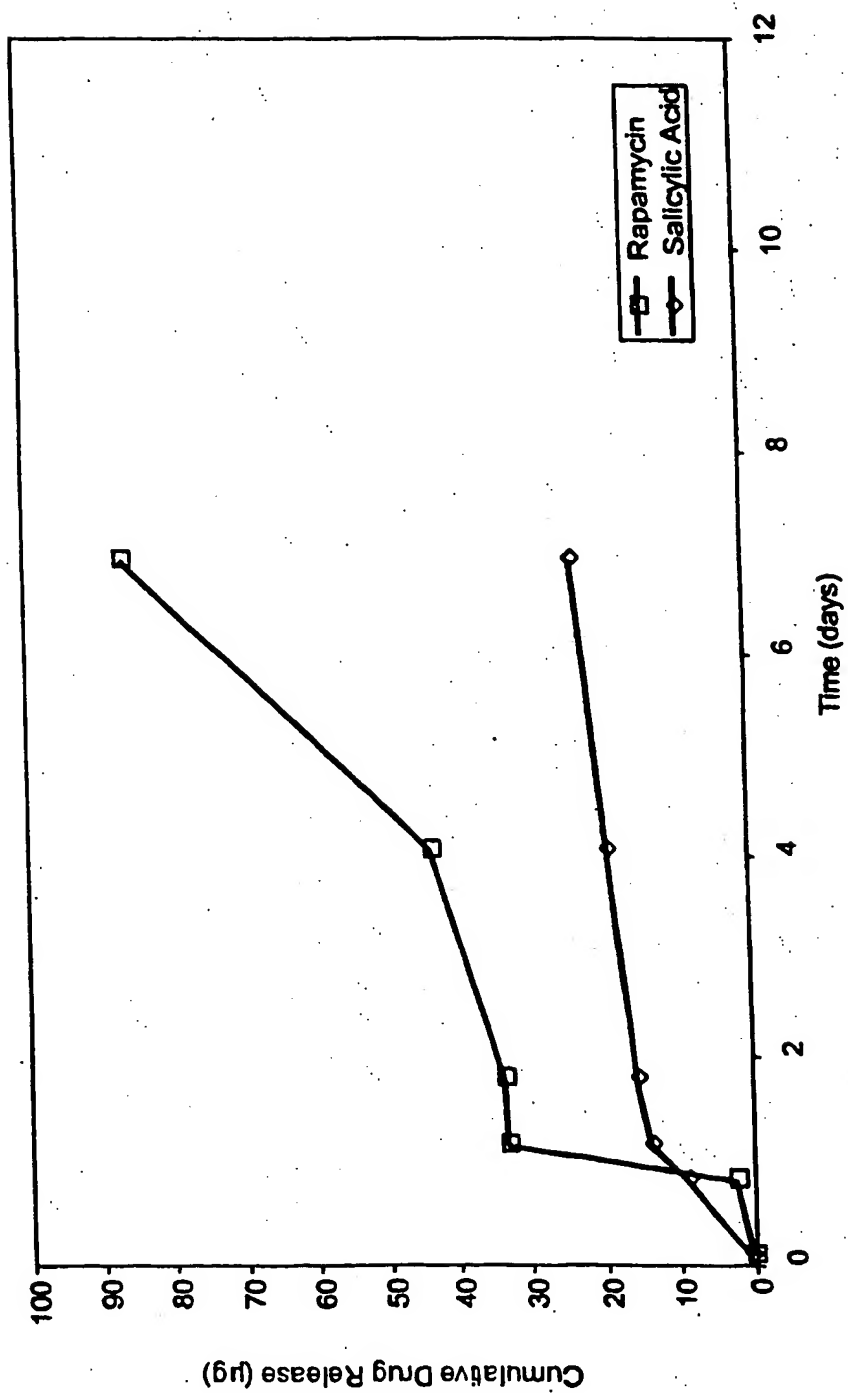


FIGURE 11

E Beam (3 MRad)		γ (25-35 KGys)			
Property	PX510	PX721	PX261	PX510	PX721 PX261
MW	-28%	-39%	-26%	-14%	N/C N/C
Hardness	-2 units	N/C	-1 unit	N/C	-3 units -2 units
Flexibility	N/C	N/C	N/C	N/C	N/C N/C
Adhesion	N/C	N/C	-1 unit	N/C	N/C N/C

N/C: no change

FIGURE 12

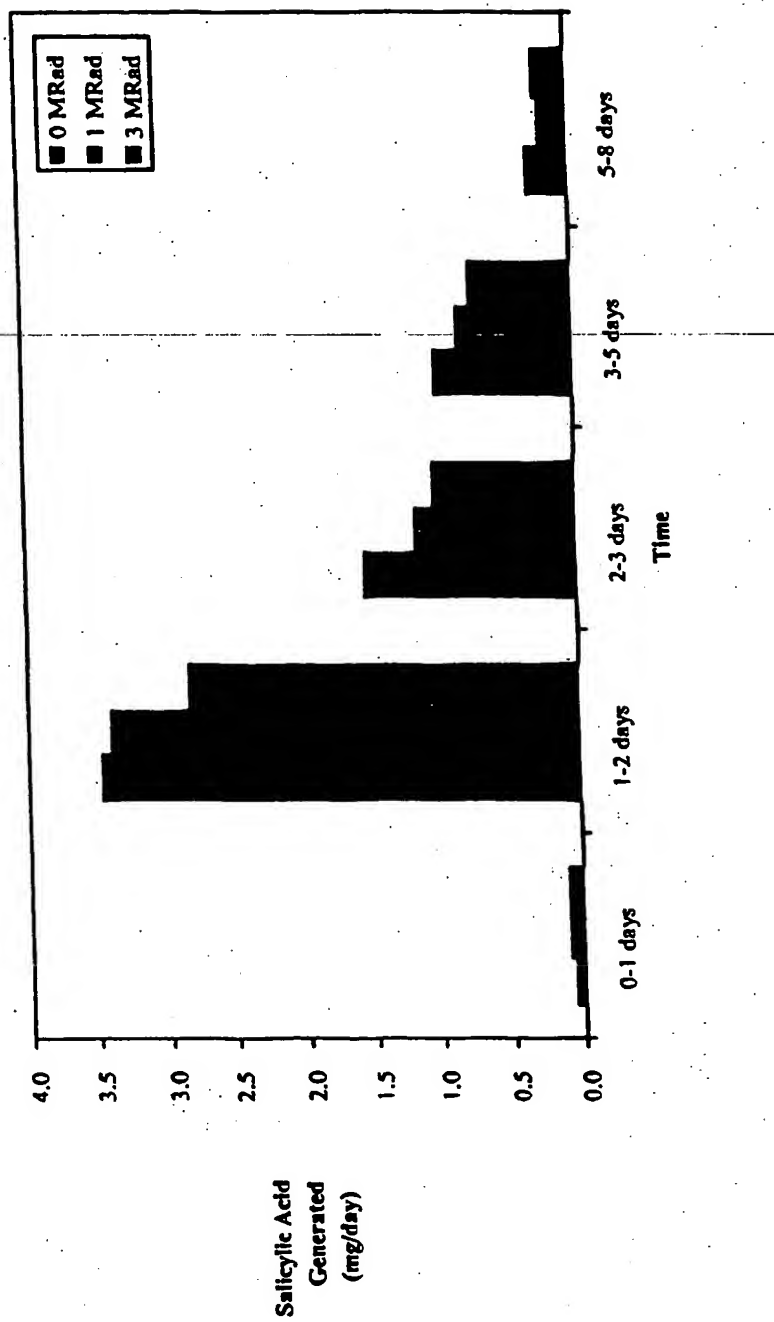


FIGURE 13A

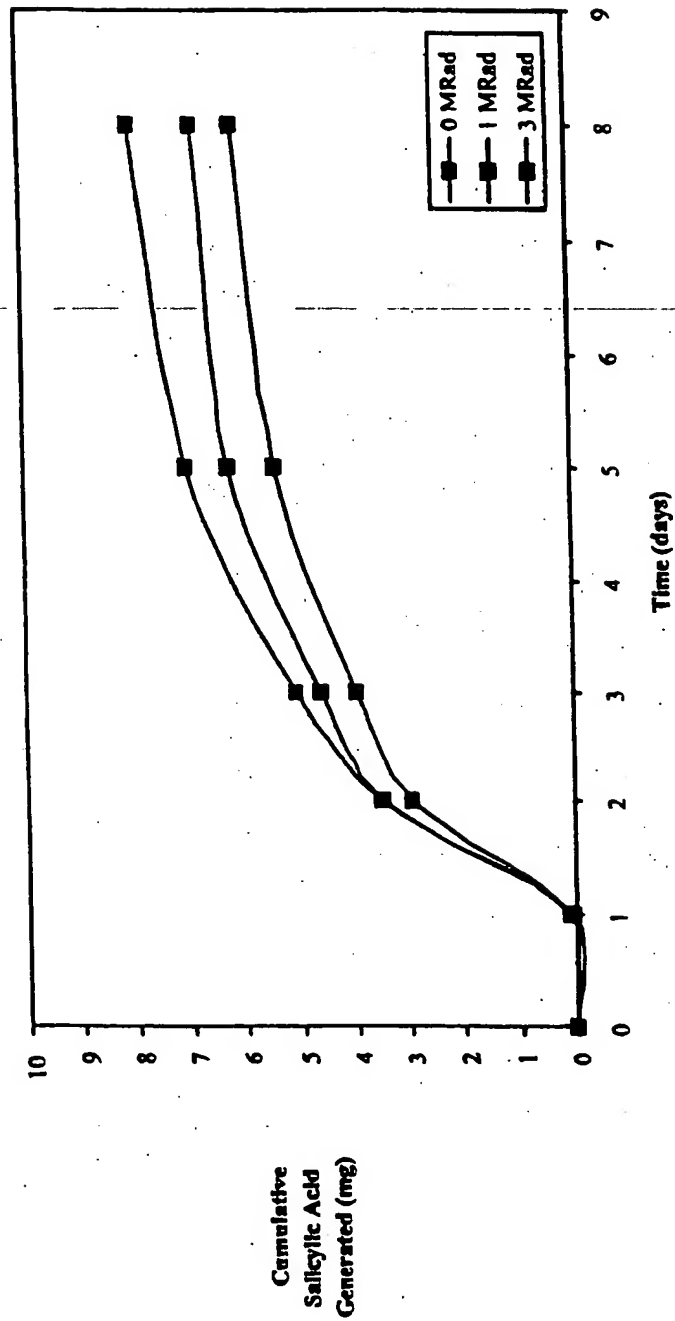


FIGURE 13B

PX242 20-53 Coated Coupon Diflunisal Elution

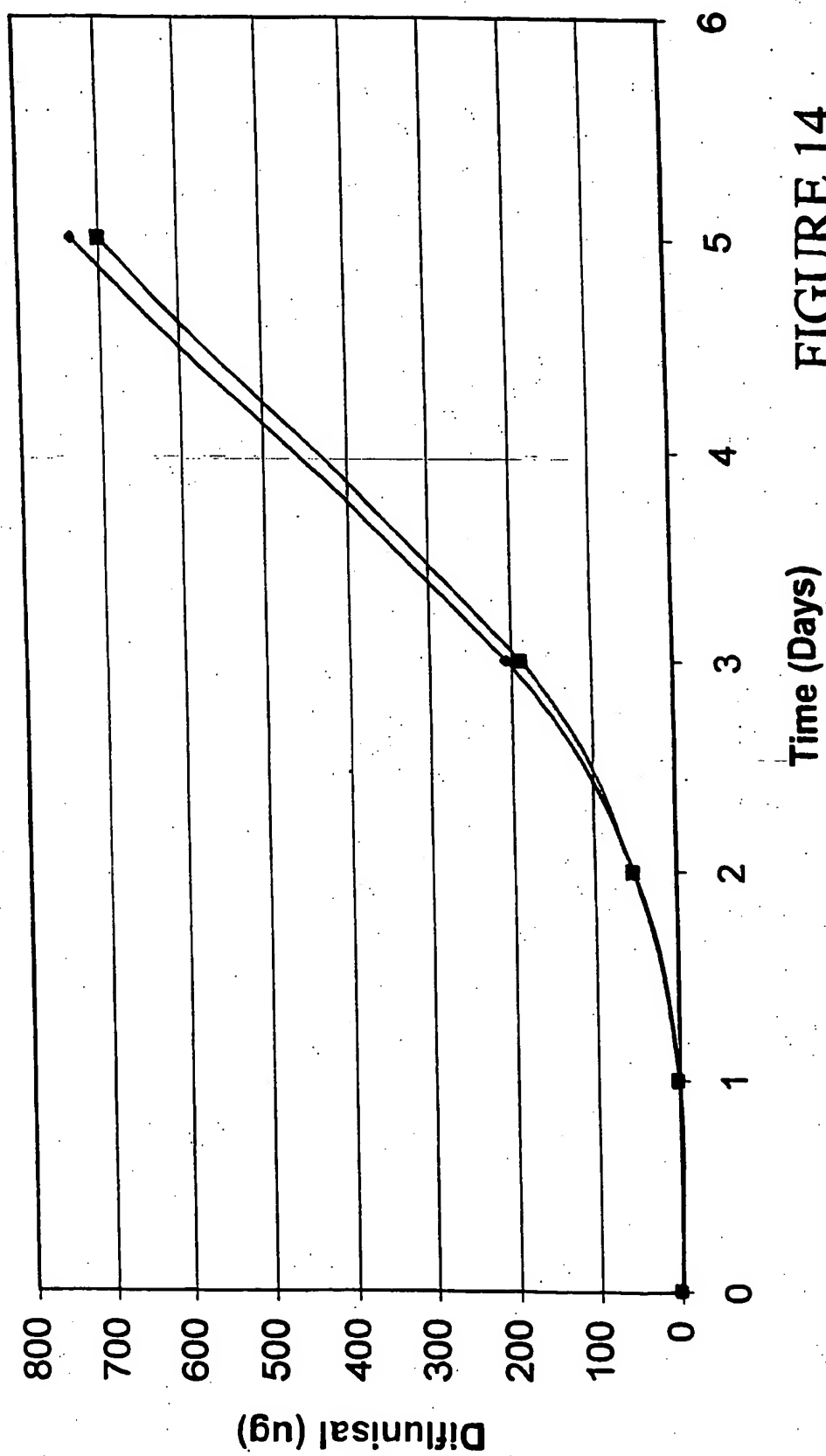


FIGURE 14

PX242 20-53 Coated Coupon Diflunisal Elution

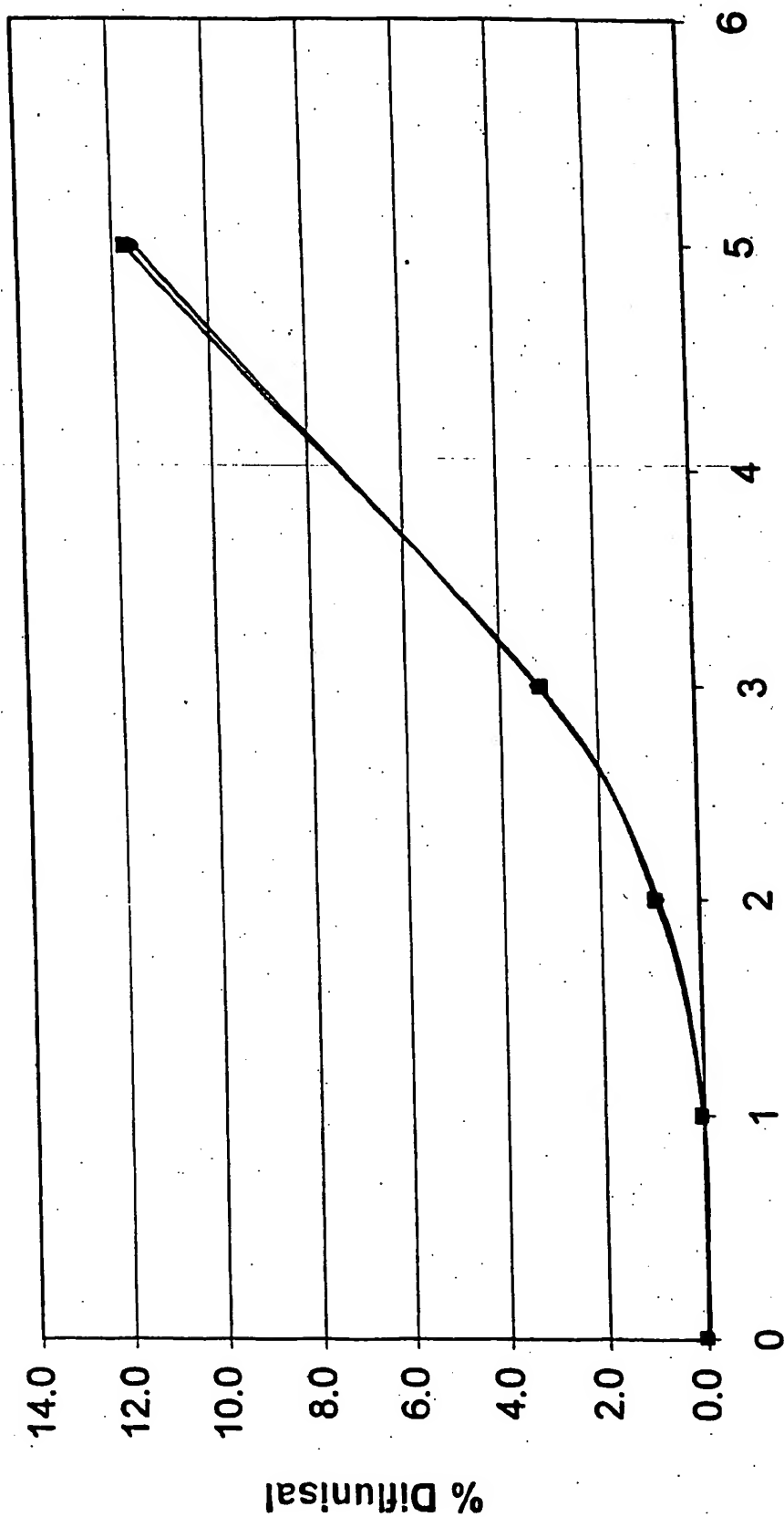
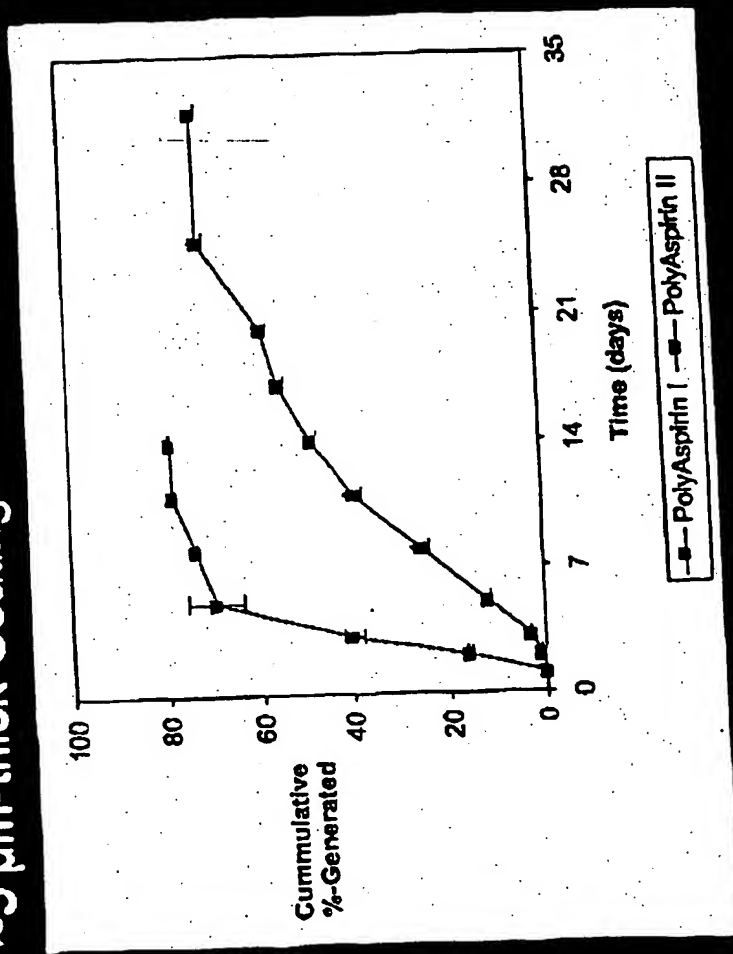


FIGURE 15

Erosion of PolyAspirin I & II

Generation of NSAID into 37 °C pH 7.4 PBS from
~5 µm-thick Coatings on 316L SS Plates

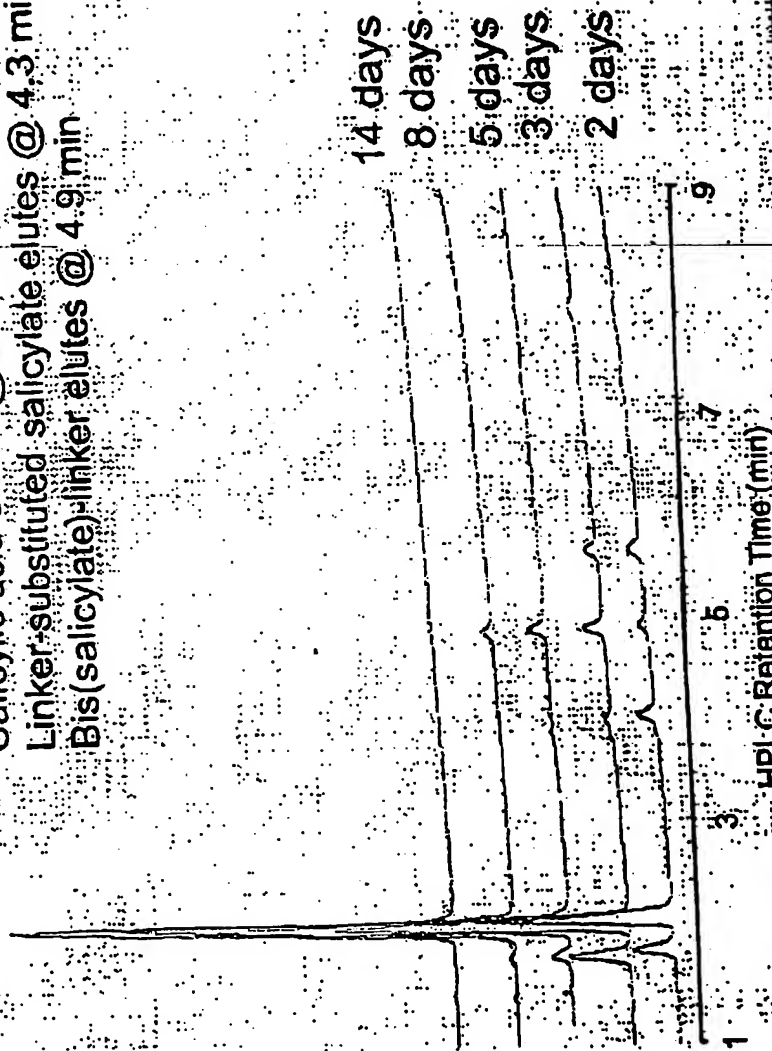


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FIG. 16

Erosion Profile for PolyAspirin I

Salicylic acid elutes @ 2.1 min
Linker-substituted salicylate elutes @ 4.3 min
Bis(salicylate)-linker elutes @ 4.9 min

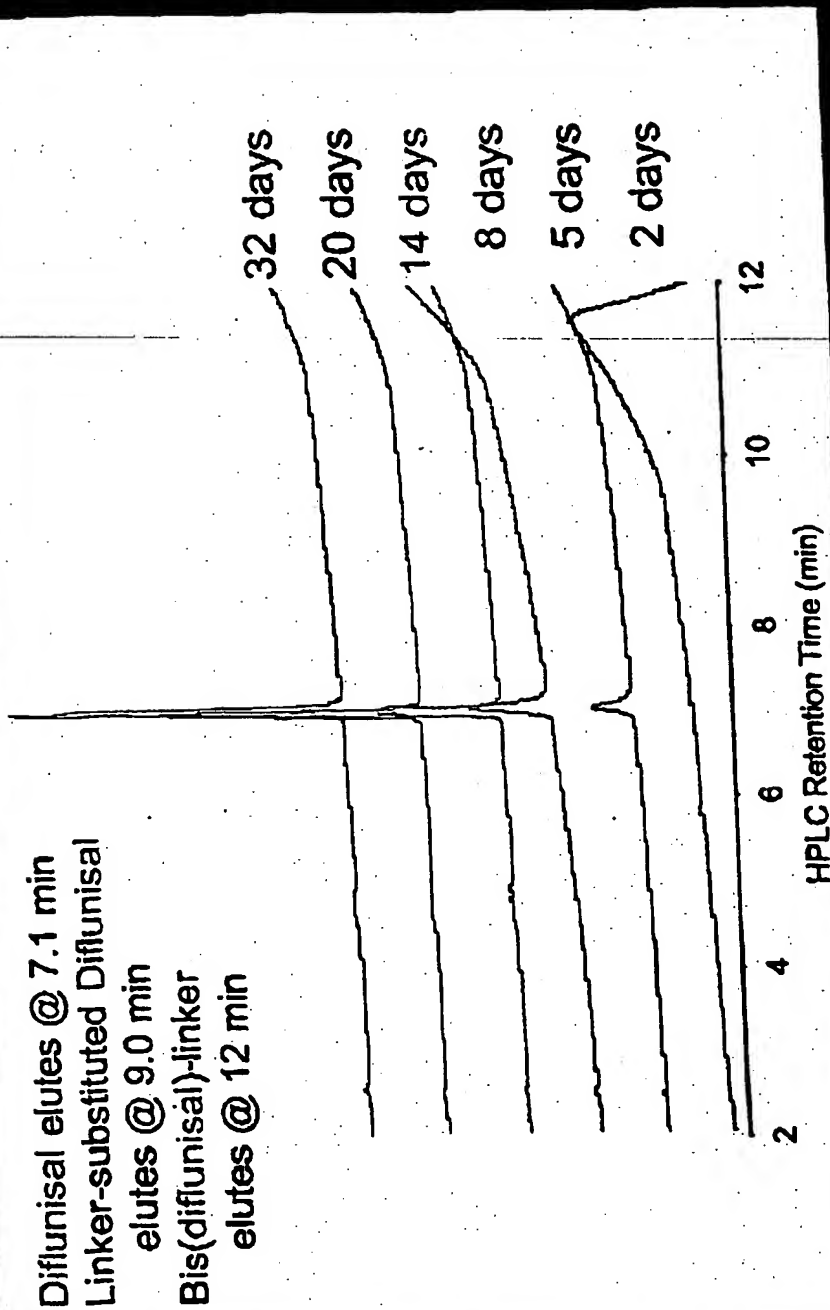


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FIG. 17

Erosion Profile for PolyAspirin II



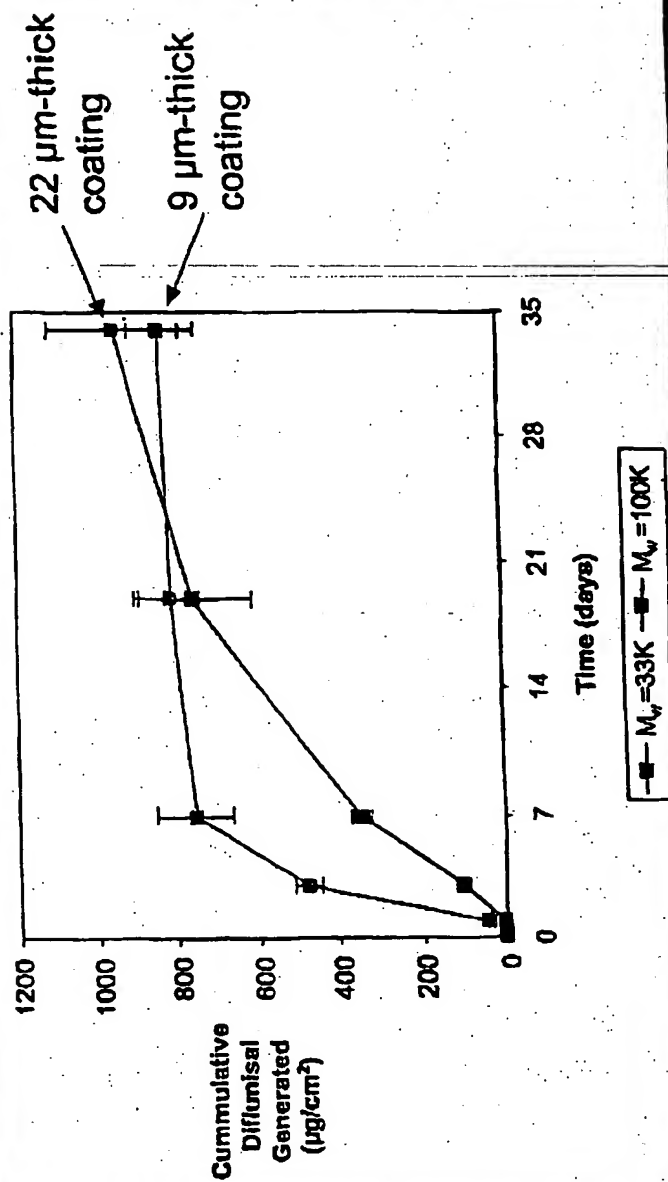
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FIG. 18

Effect of MW on Erosion

Generation of Diflunisal from PolyAspirin II into
37 °C Serum from Coatings on 316L SS Plates

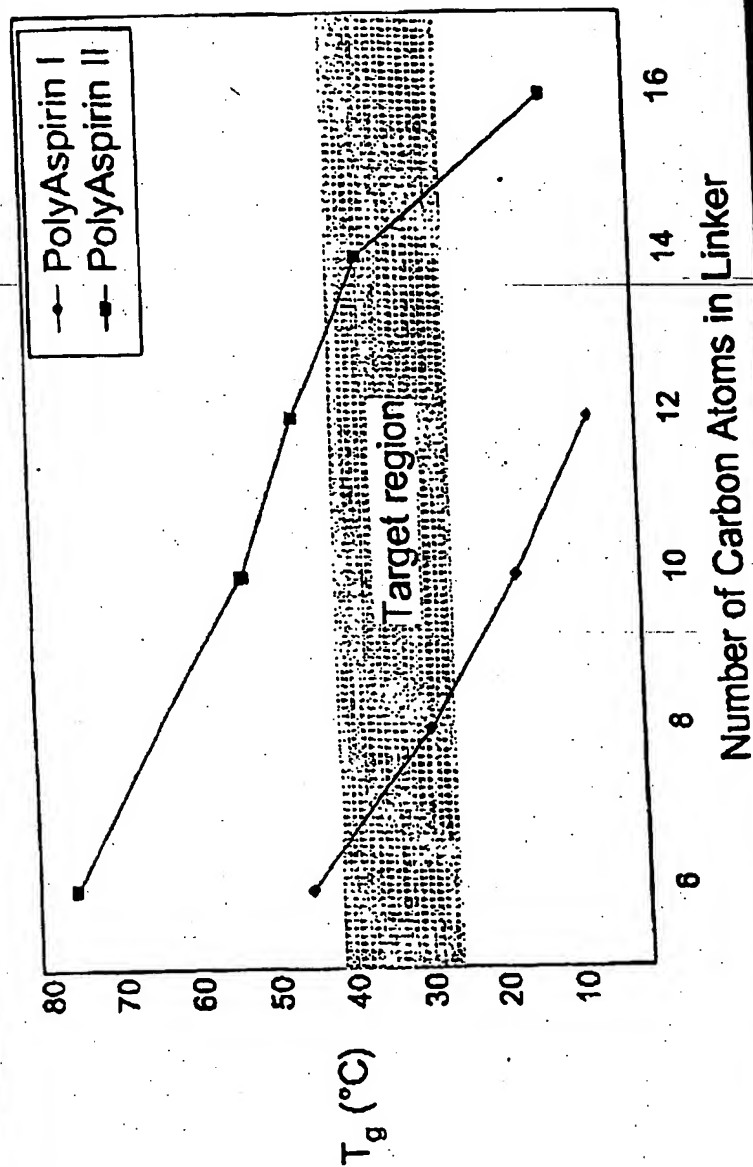


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FIG. 19

Tuning Mechanical Properties



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FIG. 20

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Thermoanalysis of PolyAspirin™

PolyAspirin I PolyAspirin II

Property	PX261	PX657
	$M_w \sim 20K$	$M_w \sim 100K$

	29	36	44
T_g (°C)			
Ultimate Stress (kPa)	1700 (25°C) >2000 (37°C)	>2800 (25°C)	>2600 (25°C)
Ultimate Elongation (%)	>500 (25°C) >500 (37°C)	>4 (25°C)	>500 (25°C)
Toughness (kPa)	>3900 (25°C) >4400 (37°C)	>560 (25°C)	>4000 (25°C)


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FIG. 21

Properties of PolyAspirin™ Coatings

PolyAspirin I PolyAspirin II

PX261	PX657
$M_w \sim 20K$	$M_w \sim 33K$
	$M_n \sim 100K$

Test

Hardness

Ambient

5 min in PBS, 37 °C

1 hr in PBS, 37 °C

3H
B
4B

F
2B
8B

Flexibility

Ambient

5 min in PBS, 37 °C

1 hr in PBS, 37 °C

<3 mm
<3 mm
<3 mm

<3 mm
<3 mm
<3 mm

Adhesion

Ambient

5B

5B

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PolyAspirin
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FIG. 22

PolyAspirin Coatings with Admixtures

PolyAspirin II (PX657)

No Admixture 20% Pacitaxel Admixed

Test

Hardness

Ambient

5 min in PBS, 37 °C
1 hr in PBS, 37 °C

F

2B

8B

F

F

8B

Flexibility

Ambient

5 min in PBS, 37 °C
1 hr in PBS, 37 °C

<3 mm

<3 mm

<3 mm

<3 mm

<3 mm

<3 mm

Adhesion

Ambient

5B

5B

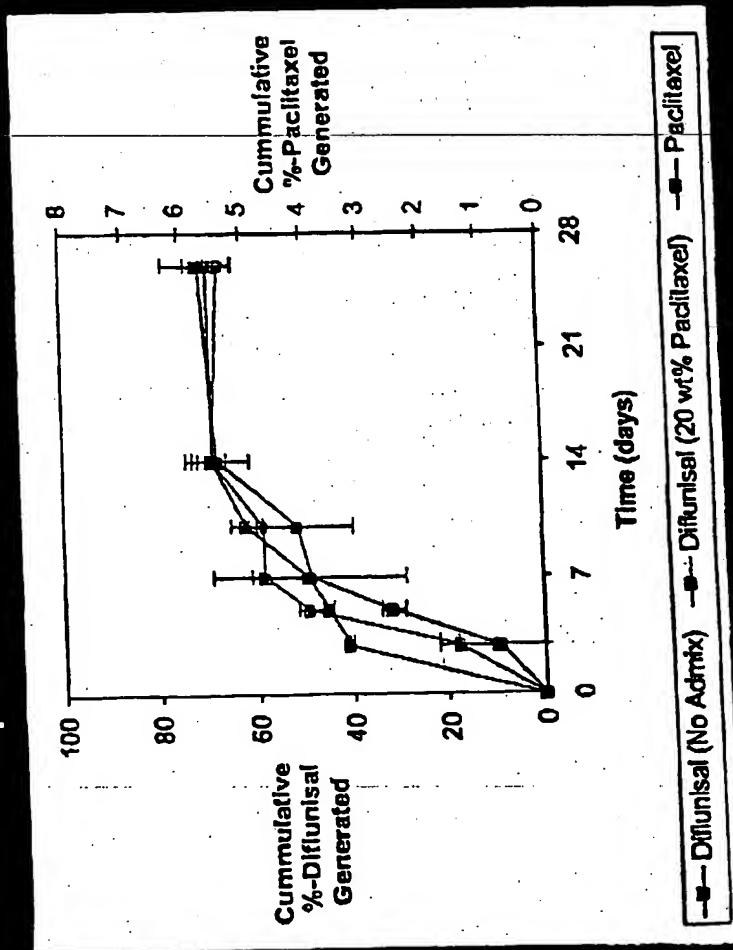
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FIG. 23

Erosion of PolyAspirin I & II

Diflunisal Generation & Pacitaxel Release into 37 °C Serum from ~5 µm-thick Coatings on 316L SS Plates

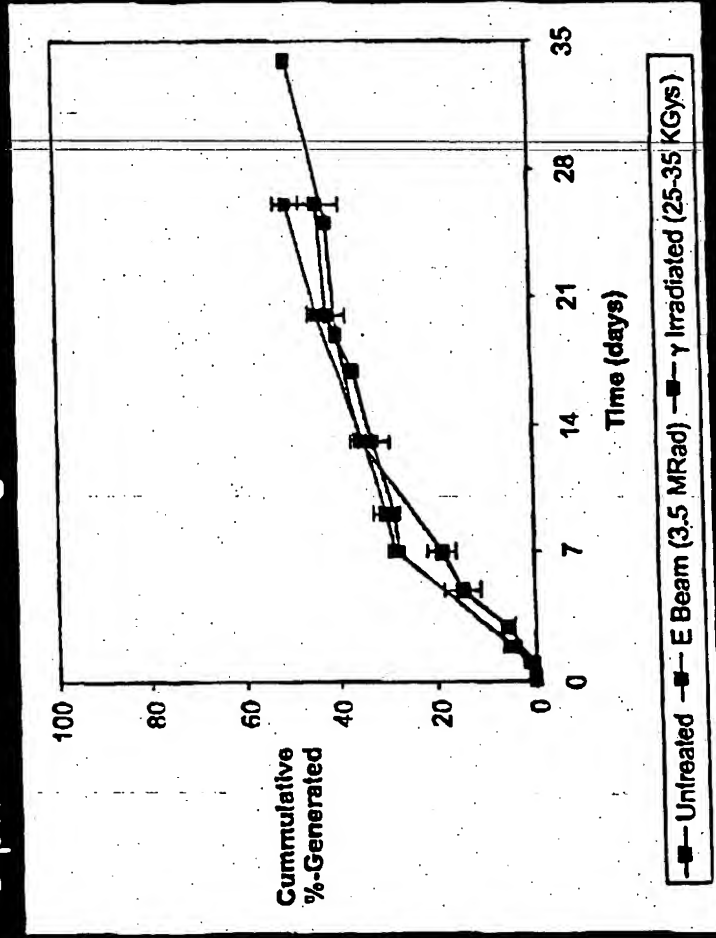


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FIG. 24

Erosion of Sterilized PolyAspirin II

Generation of Diflunisal into 37 °C Serum from
~5 μm -thick Coatings on 316L SS Plates



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FIG. 25

γ Irradiation (25-35 Kgys)

PolyAspirin I PolyAspirin II

PX261
 $M_w \sim 20K$

PX657
 $M_w \sim 100K$

Property

MW

N/C

-50%

Hardness

-2 units

-3 units

Flexibility

N/C

.

Adhesion

N/C

.

N/C: no change

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FIG. 26

E Beam (3-4.5 MRad)

PolyAspirin I PolyAspirin II

Property	PX657	
	PX261 $M_w \sim 20\text{K}$	$M_w \sim 33\text{K}$ $M_w \sim 80\text{K}$
MW	-26%	+5%
Hardness	-1 unit	+2 units
Flexibility	N/C	-
Adhesion	-1 unit	-
N/C: no change		

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FIG. 27

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Kinetics of NSAID Generation

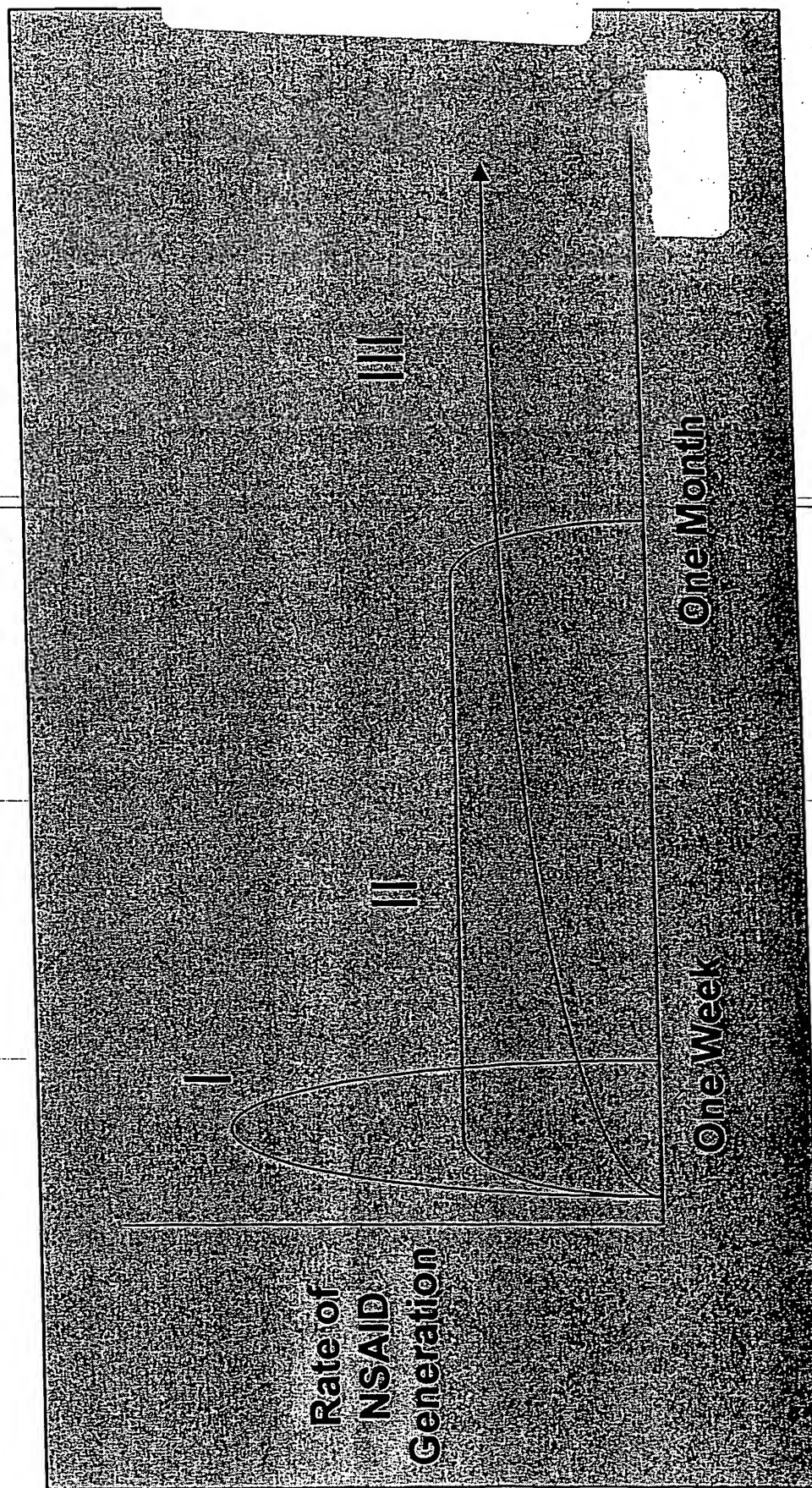


FIG. 28

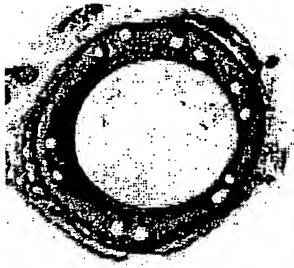


FIG. 29

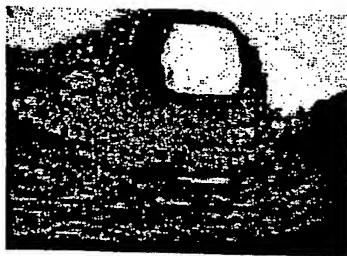
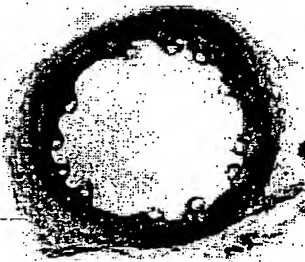


FIG. 30

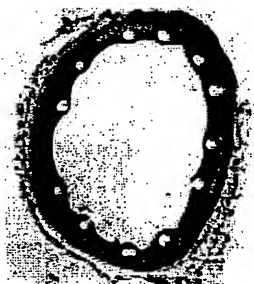


FIG. 31

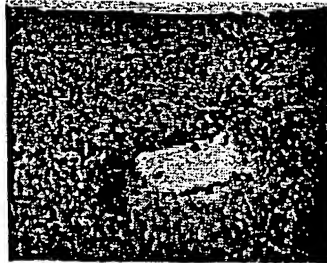
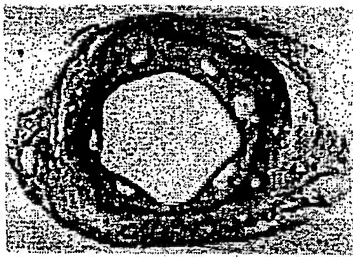


FIG. 32



FIG. 33

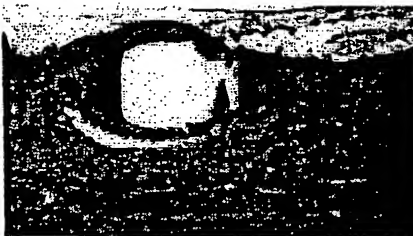
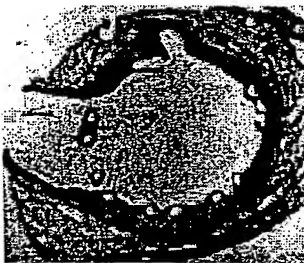


FIG. 34

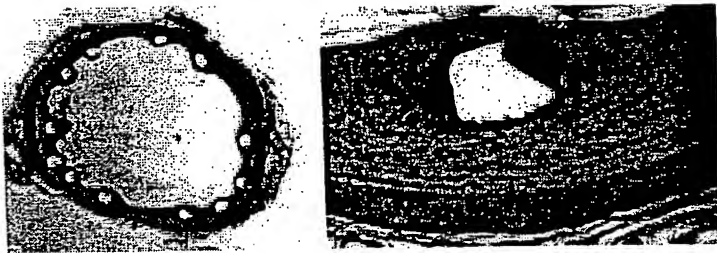


FIG. 35

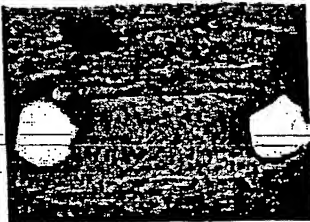


FIG. 36

FIG. 37



FIG. 38

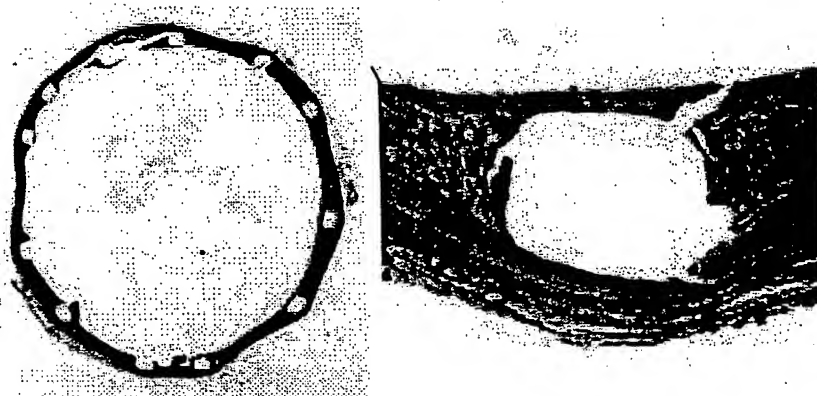
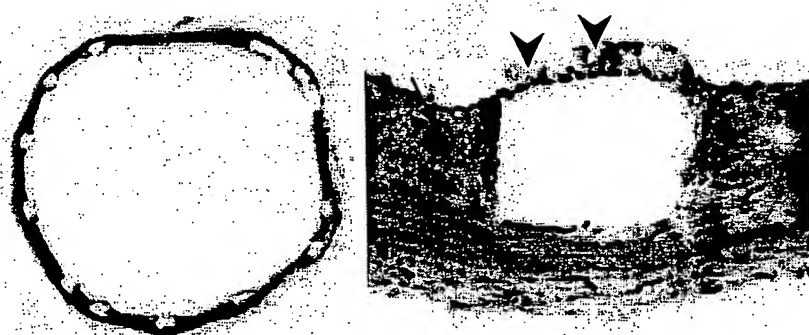


FIG. 39



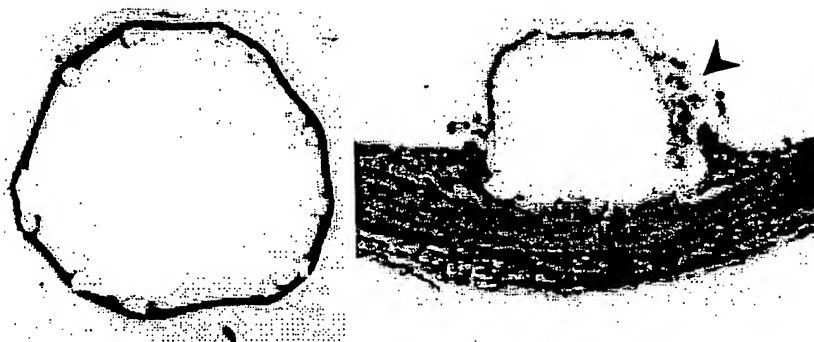


FIG. 40

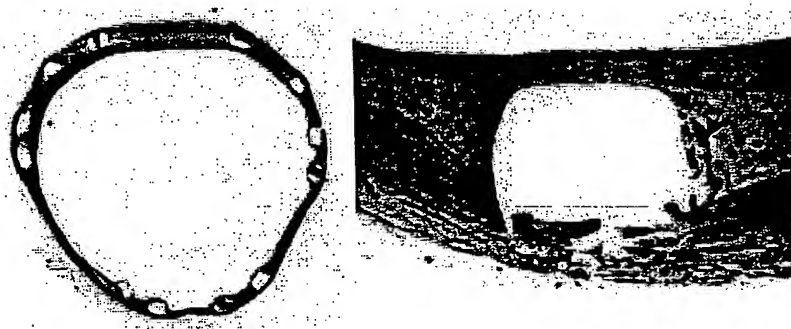


FIG. 41



FIG. 42

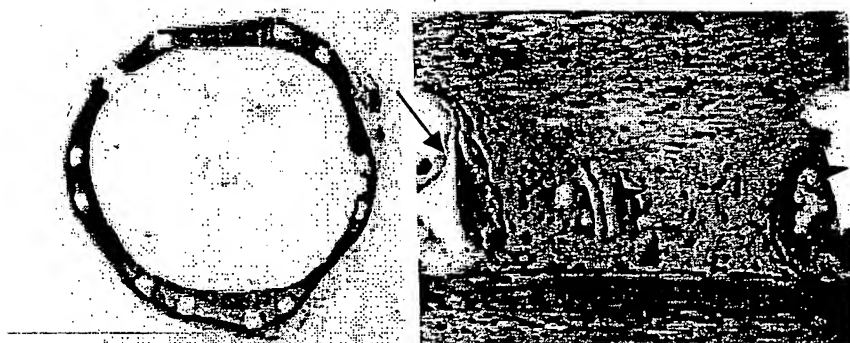


FIG. 43

uncrimped/unexpanded

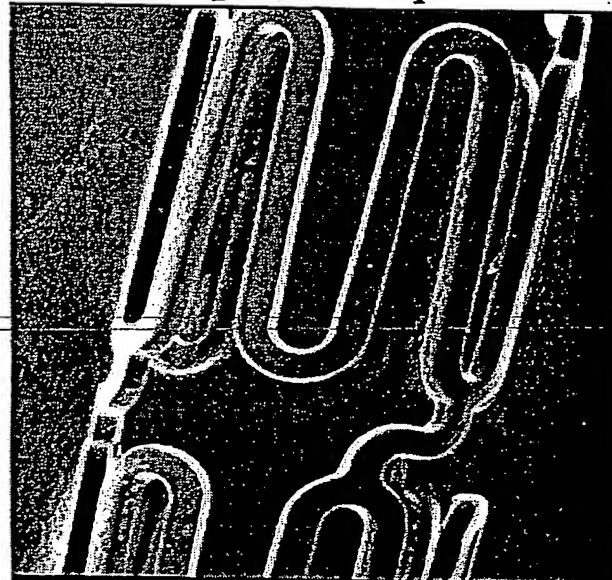


FIG. 44a

15.0 kV 1mm AMRAY



FIG. 44b

85.0x 15.0 kV 102µm AMRAY

uncrimped/unexpanded

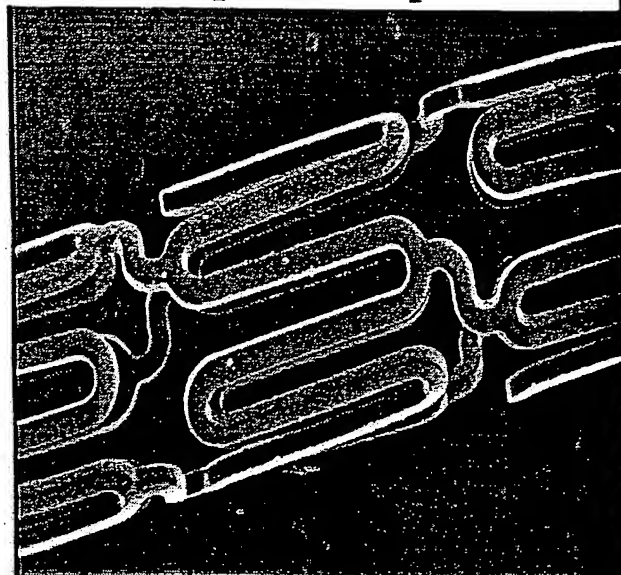


FIG. 45a

30.0k 15.0 kV 1mm AMRAY #0000

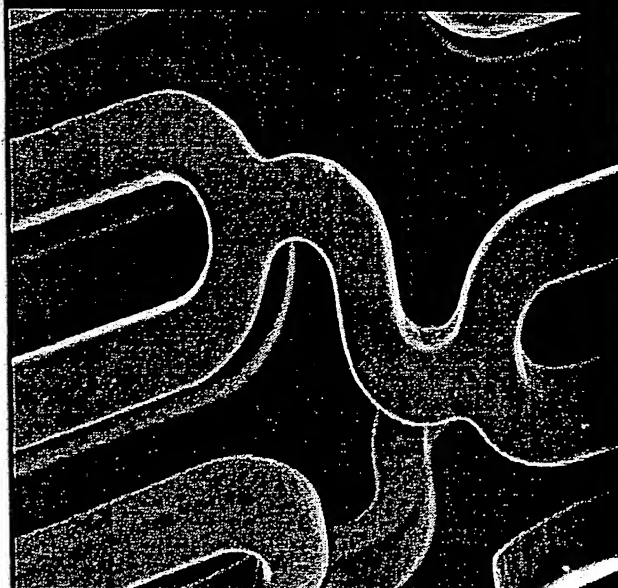


FIG. 45b

83.5k 15.0 kV 100µm AMRAY #0000

uncrimped/unexpanded

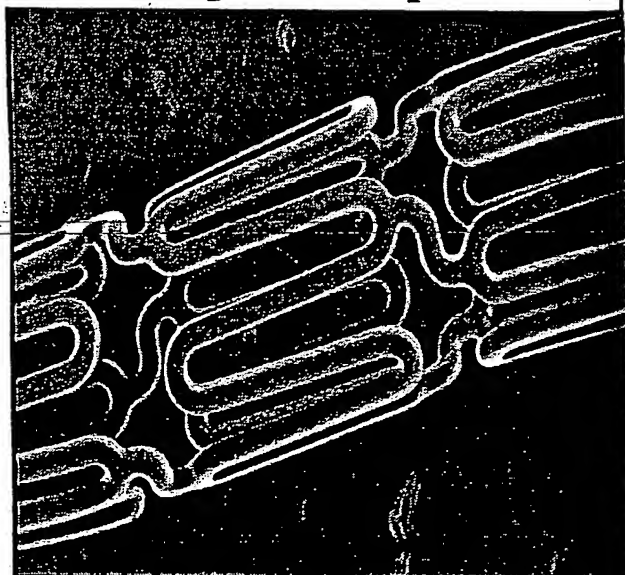


FIG. 46a

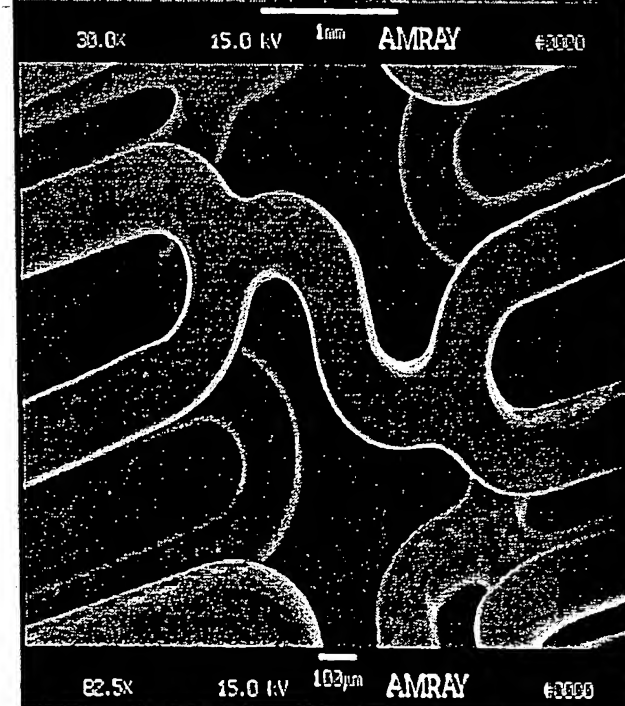


FIG. 46b

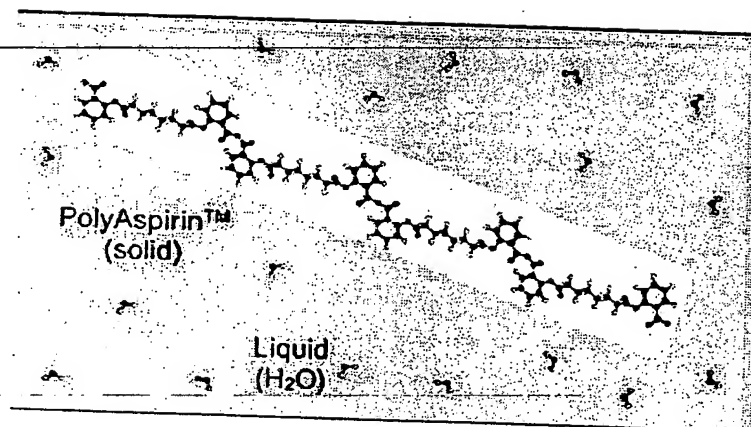


Fig. 47



Fig. 48

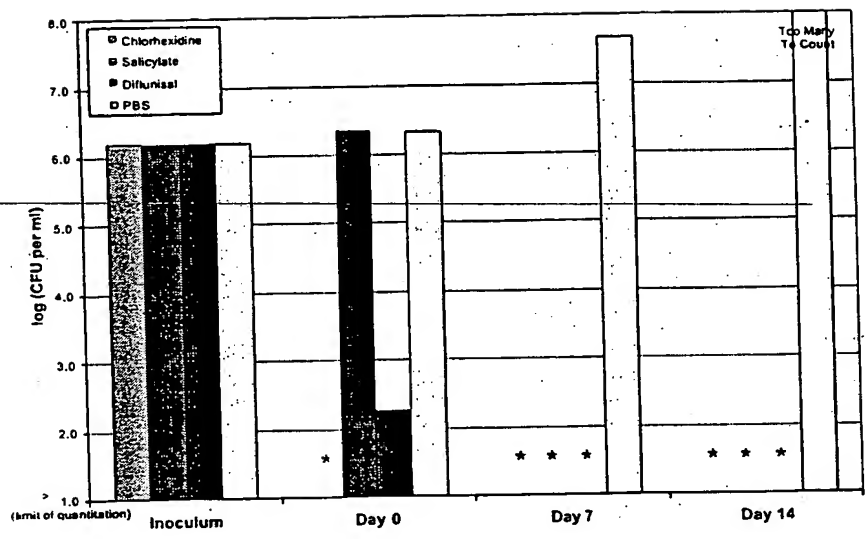


Fig. 49

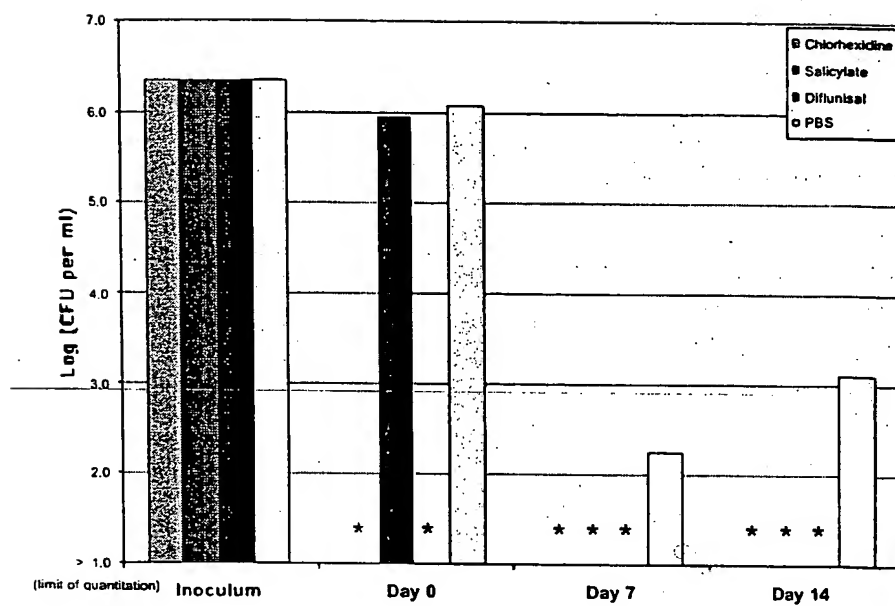


Fig. 50

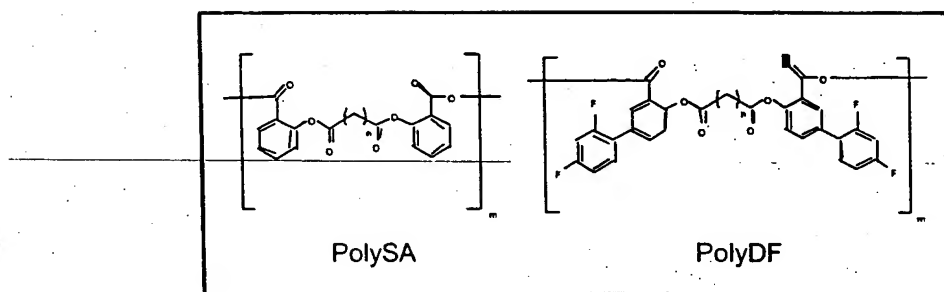


Fig. 51

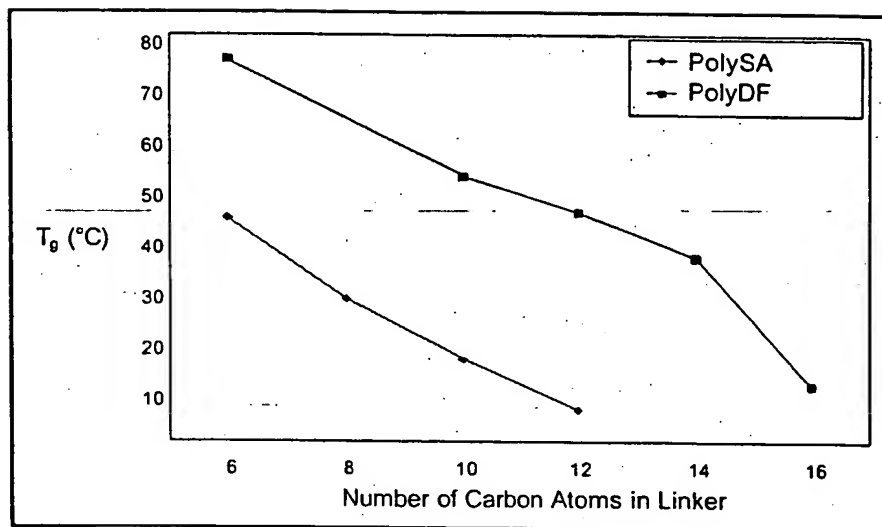


Fig. 52

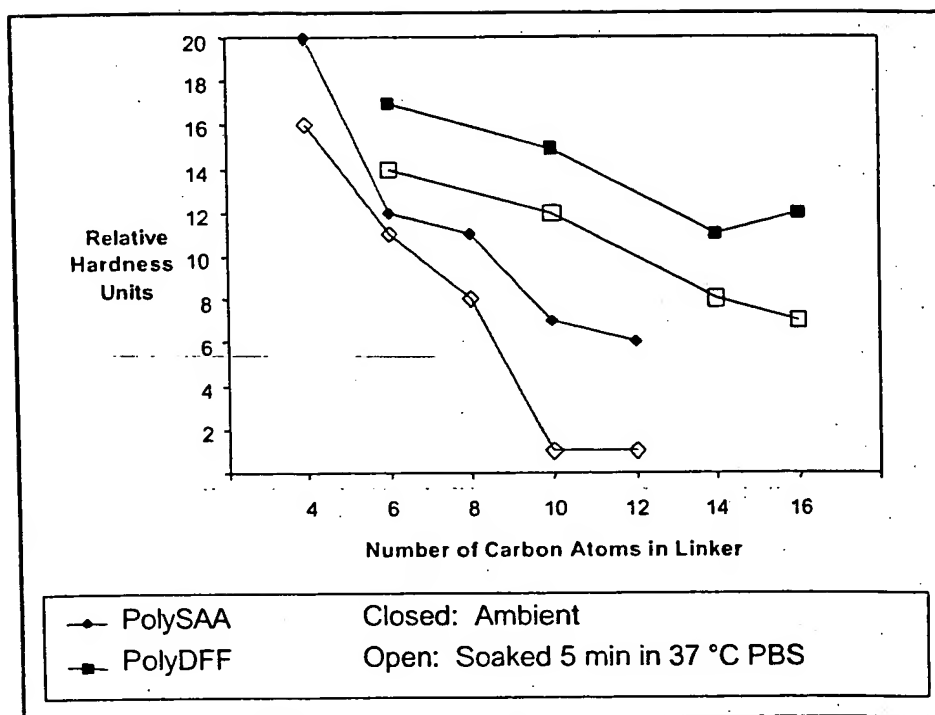


Fig. 53

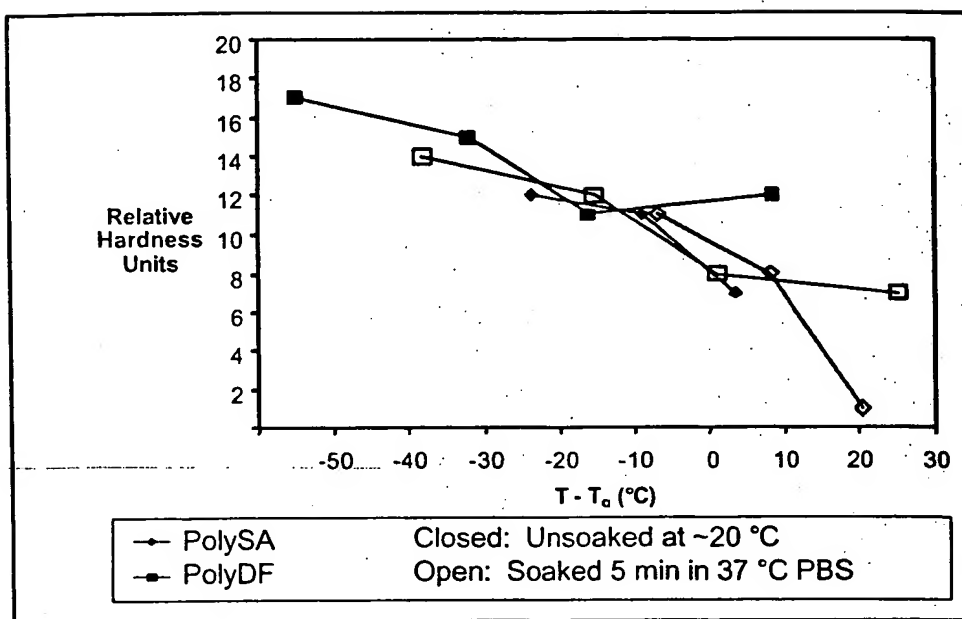


Fig. 54

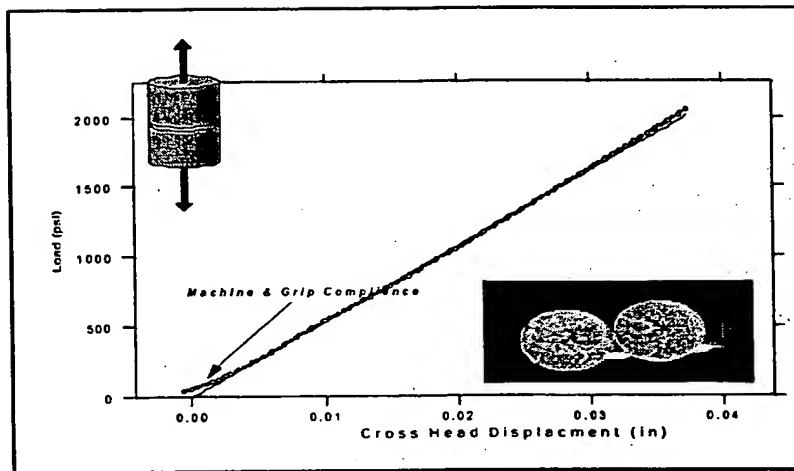


Fig. 55

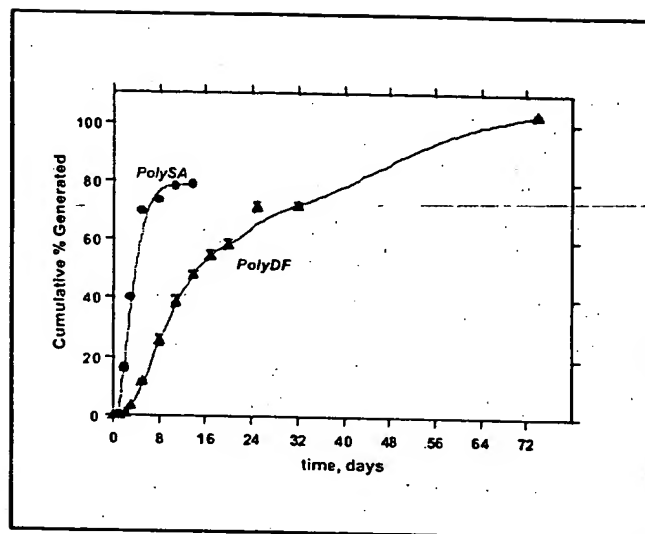


Fig. 56

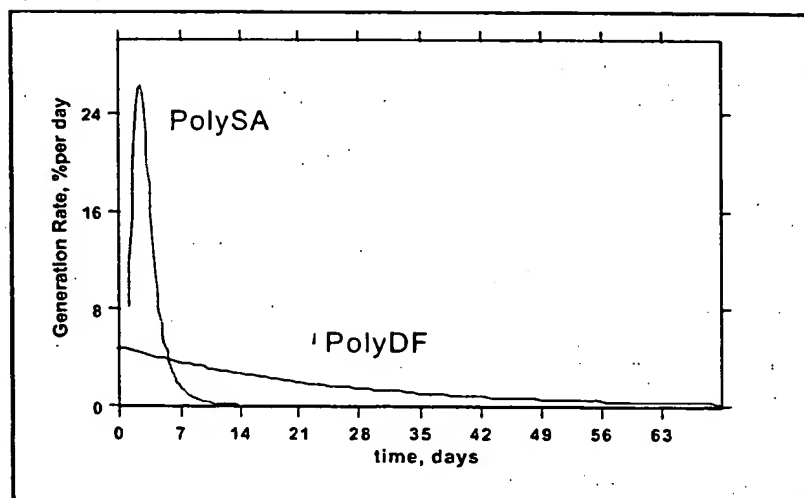


Fig. 57

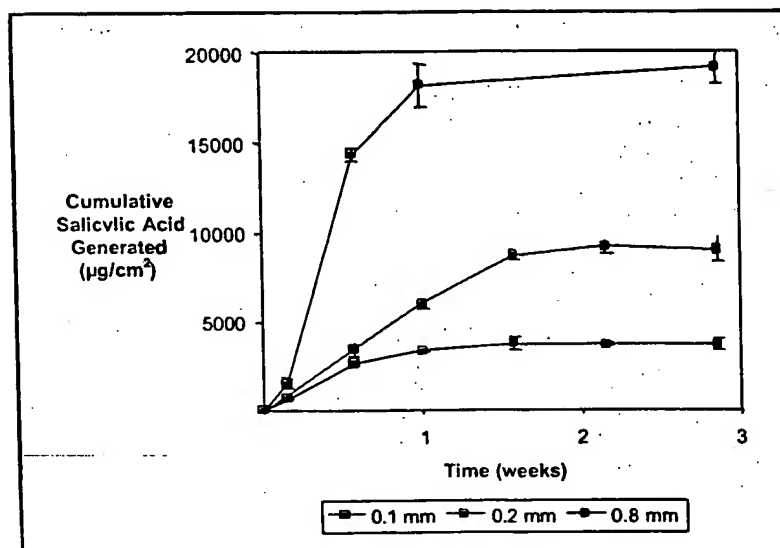


Fig. 58

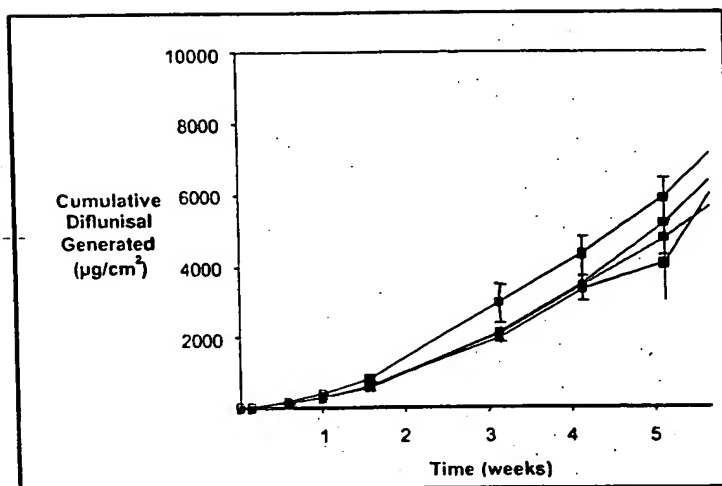


Fig. 59

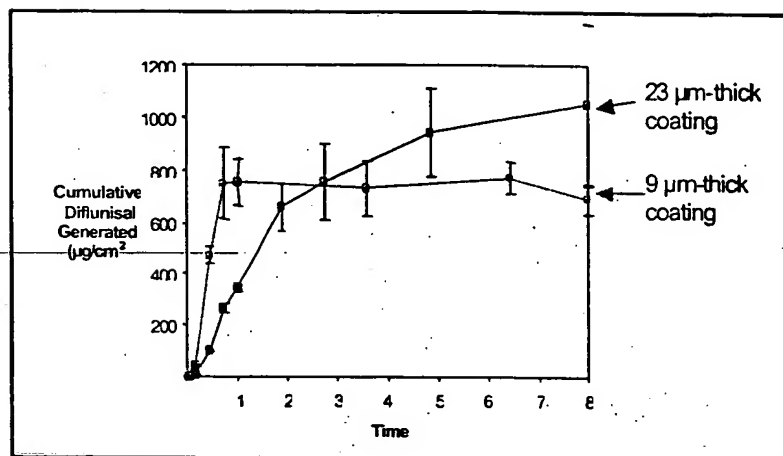


Fig. 60

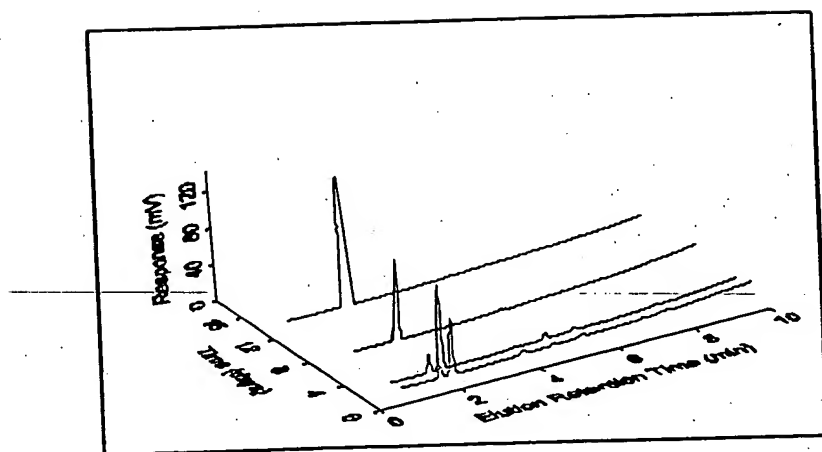


Fig. 61

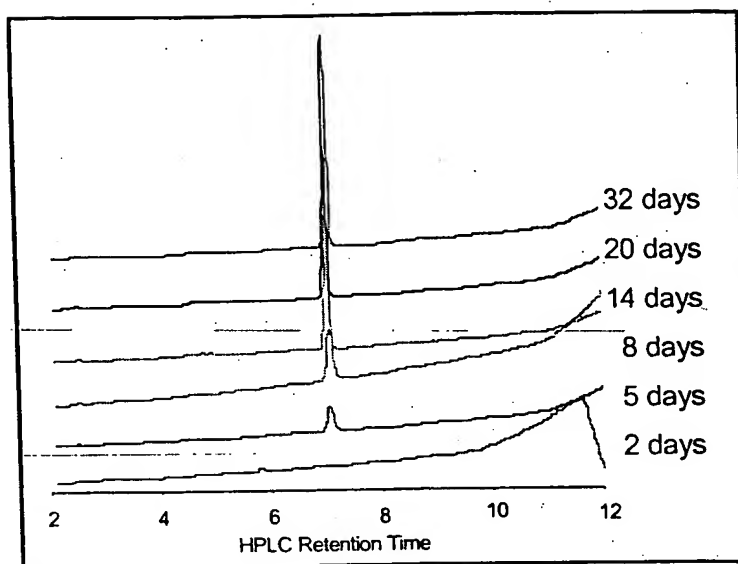


Fig. 62

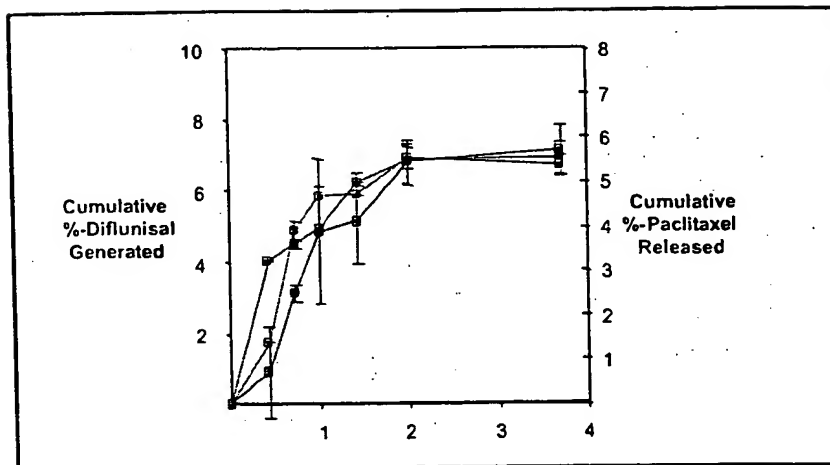


Fig. 63

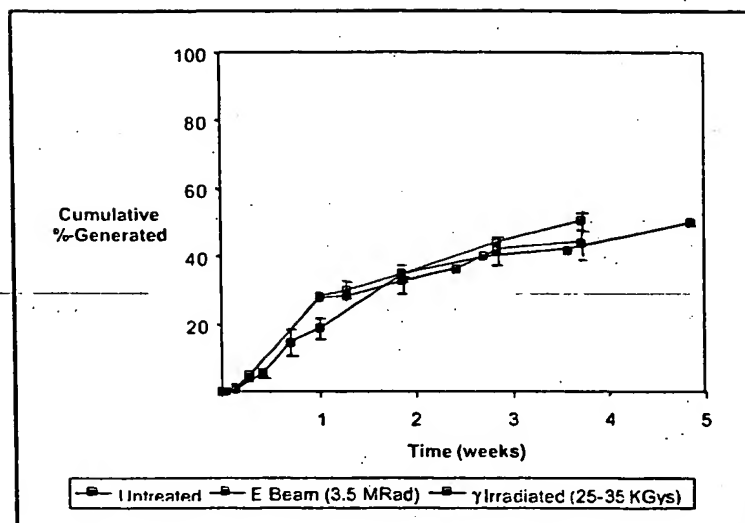


Fig. 64

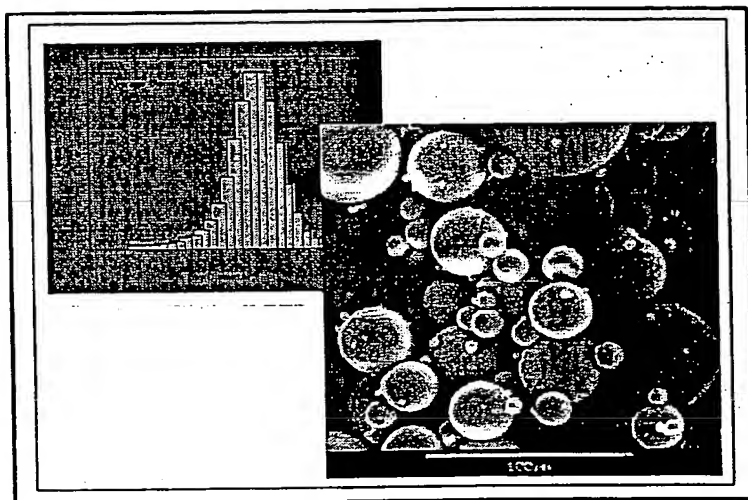


Fig. 65

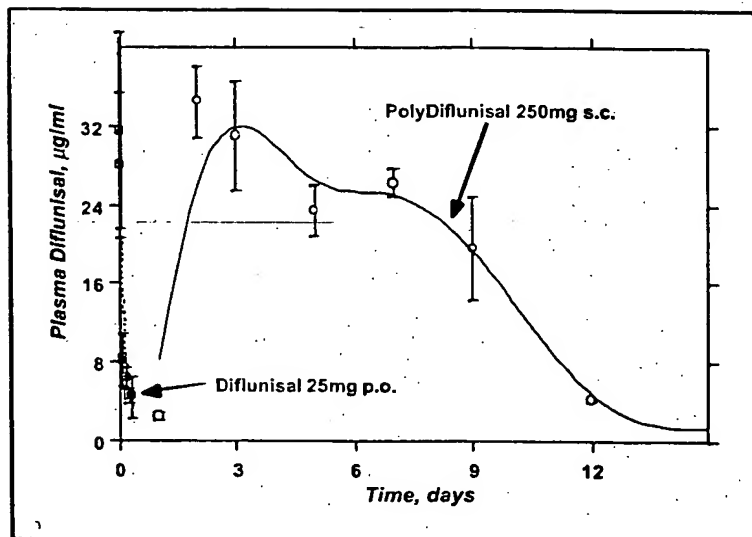


Fig. 66

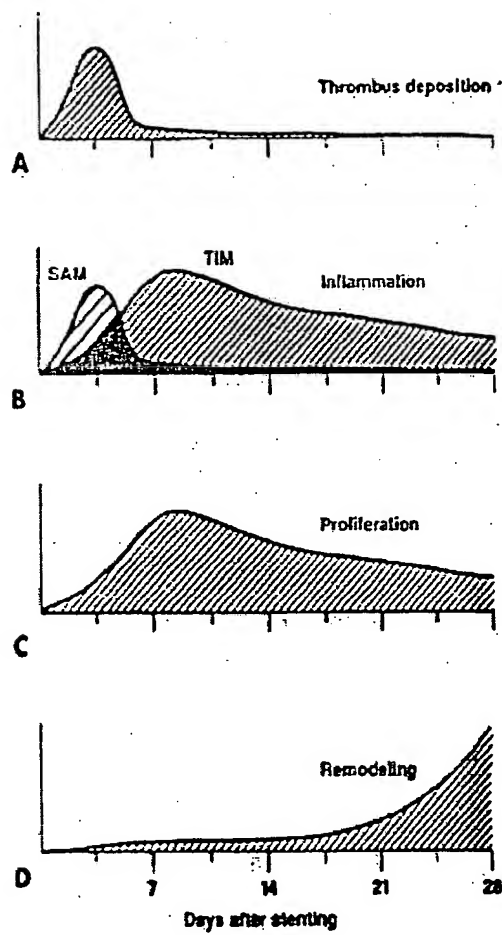


Fig. 67

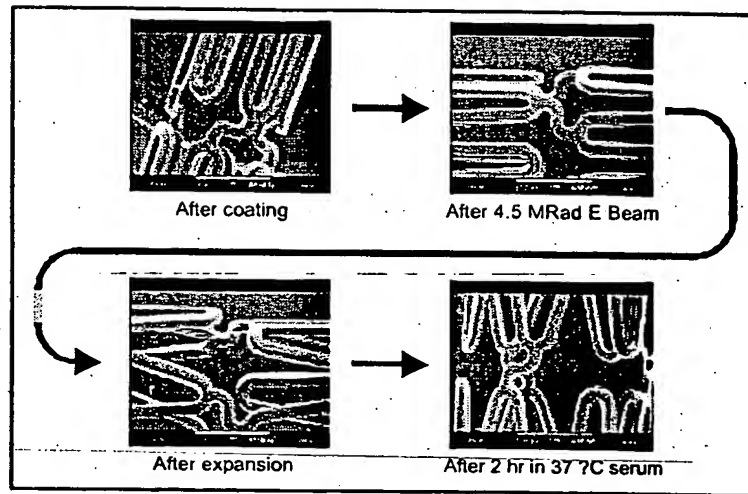


Fig. 68

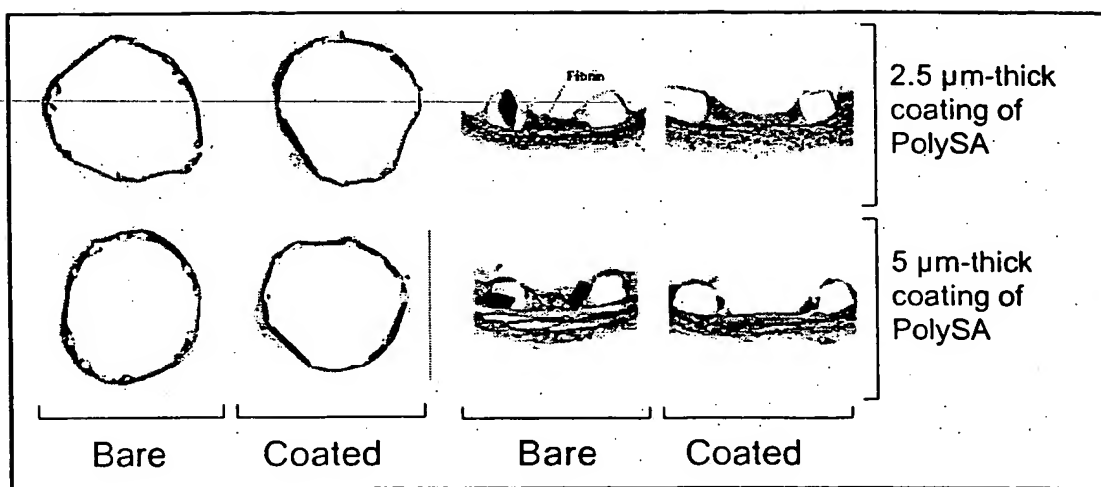


Fig. 69

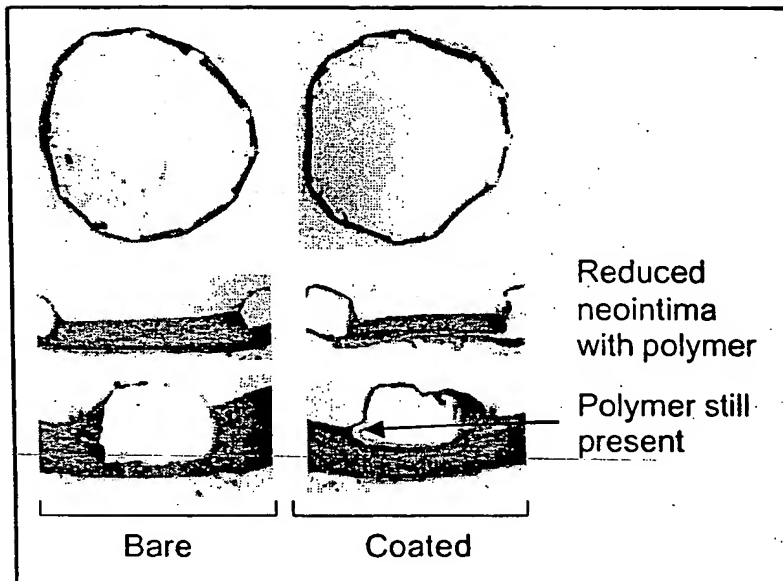


Fig. 70